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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,829	03/30/2001	Satoshi Yamamoto	12817-004001 / PH-581US-	9429

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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,829	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. The substitute specification received 14 March 2003 has been entered.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The disclosure is objected to because of the following informalities: The disclosure makes reference to several US Patent Applications but it does not reflect their current status.

Appropriate correction is required.

4. The specification is objected to as documents have been improperly incorporated by reference. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See*

General Elec. Co. v. Brenner, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As presently worded, the method of claims 1-16 encompasses the identification of any and all possible microorganisms, be they Gram negative or Gram positive, bacillus, cocci, spirochete, etc. A review of the disclosure fails to find the nucleotide sequence for any and all *gyrB* genes as found in any and all microorganisms. In order to practice the invention, one would first need to sequence the *gyrB* gene in any and all microorganisms and to have that resource at the ready in order to conduct the requisite comparison step. The specification

teaches, however, that applicant, at the time of filing, was uncertain that this gene did in fact exist, much less had been isolated and sequenced for all microorganisms. In support of this position, attention is directed to page 4,first paragraph, which states: "The genes for DNA gyrase or its isofunctional enzymes **should exist** in all organisms as they are indispensable for cell proliferation." (Emphasis added.) In short, applicant did not know, at the time of filing, if the gene existed in any and al life forms, much less provided the requisite database that is needed so to practice the claimed invention. Such non-disclosure on the part of applicant unfairly shifts the burden of enablement from applicant to that of the public. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling

> disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

While argument could be made that applicant has identified reagents to be used in the claimed method, noting "sequence pairs", which for purposes of examination have been construed to correspond to SEQ ID Nos., further review of the disclosure fails to find sufficient guidance so as to enable the claimed method to the full extent of the claims scope. It is noted with particularity that "sequence pairs (69) and (74)" re not directed to a single pair of nucleotide sequences or primers, but are directed to two oligopeptides and even then the various amino acid positions of SEQ ID NO 69 allow for 34,560 different oligopeptides. Allowing for the degeneracy of the coding sequences, applicant's SEQ ID NO. 69 encompasses 431,414,968,320 different primers, assuming that full-length sequences are used, and when combined with all possible primers that encode the various sequences of SE ID NO. 74, it is seen that there are 10,353,959,239,680 different combinations just for these two sequences. The disclosure has not provided sufficient guidance as to which of the literally trillions of possible combinations are to be used and how these results are to be interpreted. Further, the specification has not provided sufficient guidance as to how any other primer pair that encodes any other amino acid sequence is to be used in interpreting the products. At best, applicant has pointed the public in a direction of further research and has provided motivation for its conclusion. Such direction and motivation, however, have not been found to rise to the level of an enabling disclosure.

Response to Argument

7. At page 13 of the response received 14 Match 2003, applicant asserts:

> The method does not purport to identify any and all possible microorganisms by comparing the target sequence with any and all gyrB genes as found in any and all microorganisms.

An understanding or appreciation of the scope of the claims before the Office is important to the rejection. While applicant may in their response make statements that they do not now purport that the invention is to be d so widely, the claims nonetheless have just such breadth of scope. Attention is also directed to page 15 of the substitute specification (clean copy) wherein is stated:

> **Microorganisms applicable to the identification and detection method of the present invention include bacteria, yeast, Fungus, archaebacteria and the like.**

Clearly, the embodiments contemplate by applicant are non-limiting, as is evidence by the phrase "and the like." For applicant to not assert that they do not contemplate such breadth of scope has not been found persuasive or supported by the original or even the substitute disclosure.

8. As stated above in the rejection:

Allowing for the degeneracy of the coding sequences, applicant's SEQ ID NO. 69 encompasses 431,414,968,320 different primers, assuming that full-length sequences are used, and when combined with all possible primers that encode the various sequences of SE ID NO. 74, it is seen that there are 10,353,959,239,680 different combinations just for these two sequences.

9. At page 14 of the response applicant states:

> Applicants submit that although there are a large number of combinations, it is perfectly clear which degenerate DNA sequences can be used from the amino acid sequence given in the claimed method. A person of ordinary skill in the art is directed to use a pair of DNA primers from the amino acid sequences given in the claim to hybridize the primers

> to the template DNA in order to amplify the gyrB gene in a microorganism. The specification gives adequate guidance to a person of ordinary skill in the art on how to do this. Merely the fact that there are a great number to choose the primers from does not render the claimed invention non- enabling. See, for example, Yamamoto et al., *Applied and Environmental Microbiology,* Mar. 1995, 61: 1 104-1 109, submitted with the IDS dated March 30, 2001, which describes the usage of universal degenerate primers for the amplification of DNA gyrase subunit B genes. Fig. 1 can also provide guidance on the choices of the primers based on the given amino acid sequences.

While applicant may assert that it is perfectly clear to them which DNA sequences can be used from the amino acid sequence, such is not clear to the Office. At no time and at no place ahs the disclosure been found to direct the skilled artisan to which one or plurality of the 10+ trillion primes are to be used when the primers are based upon but just two amino acid sequences, much less when one contemplates using 10 amino acid sequences as recited in Claim 1.

10. In accordance with claims 1, 4-6, 8-10, and 12-16, one is to use primers predicted on the amino acid sequence of SEQ ID NO: 74. However, such a sequence presents difficulties-

Since SEQ ID NO: 74 exists also in ParE, when PCR is performed using this sequence, not only *gyrB* gene DNA fragments, but also *parE* gene DNA fragments are amplified.

(Substitute specification, page 14)

The specification, however, is effectively silent as to just which primers are to be used to identify a microorganism (claims 1—8) or to definitively detect same (claims 9-16). It is not enough that one be able to make the primers, one of skill in the art must be able to not only be able to make such primers, and their variants, but to also use same to identify virtually any microorganism, including those microorganisms that do not form perfect hybridization products and where the amplification reaction generates artifact.

11. While applicant has directed attention to the publication of Yamamoto et al., *Applied and Environmental Microbiology*, March 1995, 61:1104-1109, such an argument has not been found to be persuasive in overcoming the need of the subject application to teach in such full, clear, and concise terms such that one of skill in the art at the time the invention was made would be able to practice the full scope of the invention.

12. At page 15 of the response applicant asserts that "Claim 1 as well as other specific claims gives specific guidance as to which amino acid sequences can be used to produce the primer pairs."

13. The above argument has been fully considered and has not been found persuasive. The claims set forth what applicant considers to be the invention, and while said claims are limited to primers that are "based," in some undisclosed manner, from defined amino acid sequences, such a limitation is not considered to render the claims self-enabling.

14. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1-16 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

17. Claims 1-16 remain rejected under 35 USC 112, second paragraph, as it relates to what constitutes primers being "based" upon amino acid sequences.

Response to argument

18. At page 15 of the response applicant asserts

> The forward primer is the codes [*sic*] read off from the amino acid sequence, with provision made for codon degeneracy. The reverse primer must be converted from the coding sequence chosen from the amino acid sequence to its complement (A-> T, G->C, M->K, etc.) and then written in the reverse direction, nucleotide-by-nucleotide (not codon-by-codon). Thus that the forward and reverse primers are based on the given amino acid sequences provided in the claims would be clear and understandable to a person of ordinary skill in the art.

19. The above argument has been fully considered and has not been found persuasive. It would appear that applicant is attempting, through their remarks, to supplement the disclosure. Attention is directed to page 14 of the substitute specification wherein is stated:

> **"Primers synthesized based on sequences (a) – (l)," which are SEQ ID NOS: 69 to 80, mean primers encoding all or a part of amino acid sequences (a) – (l), and having a length sufficient to specifically hybridize to a specific site of a template DNA.**

In view of such a definition, it would appear that the primer need be based upon an amino acid sequence that need have but a single amino acid residue in common with the recited sequence, and that the primer can be of virtually any length. The definition does not identify any metes and bounds to the degree of homology that must exist in order to arrive at sufficient hybridization conditions or to allow for efficient priming and amplification. Rather than "particularly pointing out and distinctly claiming" how these primers are "based" upon the recited amino acid sequences, such description is left up to the public to determine.

20. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

21. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

22. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

25. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
July 8, 2003